

Update on Alzheimer's



Using Nonevidence-based Approaches to Treat Patients with Alzheimer's Disease

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ABSTRACT

In this article, the author discusses the rationale behind offering patients with Alzheimer's disease treatments that are not strongly evidence based. The author will discuss specific nonevidence-based (or not strongly evidence-based) interventions psychiatrists may consider offering

their patients with AD, including nonpharmacological and pharmacological approaches. The author will also discuss positive and negative aspects of these interventions and suggest some steps psychiatrists can take to try to avoid the potential downsides.

KEY WORDS

Alzheimer's disease, patient autonomy, nonpharmacological intervention, pharmacological intervention, research protocol, ethics

INTRODUCTION

Psychiatrists treating patients with Alzheimer's disease (AD) seek to help each patient as much as they can, but interventions proven to be beneficial, such as cholinesterase inhibitors and memantine, offer only limited benefits. Due to this and to the devastating effects of AD, psychiatrists may consider using interventions that are not strongly evidence-based, especially if patients and/or their caregivers want this. In this article, I will discuss the rationale behind offering patients treatments that are not strongly evidence based. I will also discuss specific nonevidence-based (or not strongly evidence-based) interventions psychiatrists may consider offering their patients with AD, including nonpharmacological and pharmacological approaches. I will discuss positive and negative aspects of these interventions and suggest some steps psychiatrists can take to try to avoid the potential downsides.

WHY RECOMMEND APPROACHES THAT ARE NOT STRONGLY EVIDENCE-BASED?

There are many levels of evidence, ranging from randomized, controlled, double-blind trials and overviews or meta-analyses based on these data to observational studies, expert opinions, case series, case reports, and studies with historical controls.¹ Treatment decisions for patients with AD may become increasingly difficult as the evidence base of certain treatments becomes weaker. Psychiatrists, however, may want to use some interventions in spite of their weaker evidence base.

Due to the devastating nature of AD, psychiatrists may be more inclined to try to help patients with AD in any way they can compared to physicians treating patients with other medical conditions. The willingness to try different interventions at the request of the patient, even those interventions that do not have a strong evidence base, demonstrates that the psychiatrist has respect for the patient's autonomy. Psychiatrists show respect for patient autonomy in a similar way when they adopt a sliding scale in determining patients' decision-making capacities.

When a patient has a particularly serious illness, such as terminal cancer, his or her only choices may be to take a third or fourth trial of chemotherapy, which could increase his or her life only a few months, or to stop treatment altogether. Medicine in a case like this has less to offer the patient, but the physician can still offer the patient the choice of whether or not to undergo another round of chemotherapy. In patients with AD, allowing them to make similar choices, even when they are significantly cognitively impaired, respects their autonomy to a greater extent. These patients may want to participate in drug trials, for example, because it gives them hope. This hope is not unrealistic. After all, these interventions, though less evidence-based, *may* help.

There is a risk that offering off-label or nonevidenced-based therapy choices may give a patient false hope, even if the patient is accurately informed that it is unlikely that he or she will benefit from the treatment. The risk of false hope is likely to be increased in patients with AD because their cognition is impaired. This particularly may be the case if the patient with AD is also depressed. Some patients may feel, for example, that they will do

anything if it would help.

Accordingly, some psychiatrists fear that even only informing patients with AD of an option that does not have a strong evidence base, much less offering this intervention to the patients, is contraindicated because of the risk of false hope, which may interfere with the patient trying to maximize the quality of his or her life in other ways, while he or she still can. This rationale of not informing patients of options less evidence-based presupposes, however, that for these patients having this hope and concomitantly seeking the greatest quality for their lives are mutually exclusive. This may not be the case. It may be that these patients can have it both ways, and psychiatrists may be able to facilitate this by informing patients unequivocally that they should expect no benefit but possibly may be surprised.

Though the caregiver of a patient with AD may not be cognitively impaired, he or she is also subjected to the risk of false hope. The concerns of the psychiatrist related to patients with AD apply to caregivers as well. A problem may arise if a patient with AD wants a nonevidence-based intervention but his or her caregiver does not want the patient to get it or if this situation is reversed, which may especially be the case if a patient's decision-making capacity is significantly impaired. In this case, a patient with AD may be capable of only giving assent. Psychiatrists in these instances may be tempted to defer to the caregiver for the treatment decisions. Though a caregiver may be legally authorized to make treatment decisions for a patient with AD, clinically and ethically it may be a mistake for a psychiatrist to defer to the caregiver. Clearly, a patient with AD, like an older child, should be generally able to refuse an intervention even when

his or her decision-making capacity is impaired. A request by the patient to have a treatment may warrant similar weight, even when he or she is cognitively impaired.

A psychiatrist should, therefore, consider such patients' preferences as well as their needs. To respect patients with AD and their preferences, psychiatrists should optimally try to infer their needs and wants, even when the patients do not or cannot express them explicitly. For example, an 87-year old woman with moderate AD did poorly upon first entering a nursing home; she ate very little, showed behavioral expressions of anxiety, such as hand-wringing, had disrupted sleep, and stayed physically and emotionally isolated. Even though the patient ate little, she constantly talked about food. The daughter wondered if this "obsessing" over food was because she missed the mealtime rituals with her family. Thus, her family started to visit her during mealtimes whenever possible. They also brought foods they knew she loved. The patient responded well to this change by eating more, becoming less anxious, decreasing obsessive reminiscence, and, in general, making a smoother transition into the nursing home environment.²

NONPHARMACOLOGIC INTERVENTIONS

Exercise. Exercise may benefit patients with AD in many ways.³⁻⁶ It may positively affect their physical and emotional health as well as possibly their AD. It may, for example, even improve cognition.⁵ The biggest challenge for these patients is to establish a regular exercise routine they enjoy and are able to maintain on a consistent basis. For example, patients may be more willing to use a stationary bike every day at the same time if they can simultaneously watch one of

their favorite shows on television. I knew a patient who loved watching football, even though he never knew who was playing or what the score was. This created an excellent opportunity for him to use a treadmill during the games. Patients with AD also may be more likely to continue an exercise routine if they and their caregivers or significant others can do it together. This is particularly helpful with spouses or other family members with whom patients with AD have lived for many years.

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What then could possibly be a downside to an exercise prescription? Patients with AD may choose not to continue regular exercise for many reasons, including increased feelings of apathy. If a patient with AD wants to stop regularly exercising, his or her caregiver may feel compelled, as a result, to push the patient against the patient's wishes to continue the exercise routine, or the caregiver may feel guilty and responsible if the patient stops.⁷ Either result may harm the patient/caregiver relationship, and this relationship may possibly be the most important thing in the patient's life. Psychiatrists can reduce these risks by discussing them openly with the patients and their caregivers before prescribing the intervention.

Increasing social interactions.

It may be very beneficial for patients with AD to continue to have social

interactions as much as possible.^{8,9} It is unclear why increasing the social interactions of patients with AD may help, but, even at more severe stages of AD, increased interactions may benefit their cognition.⁹ However, these interactions may cause greater stress for the patient. Patients with AD may find, for example, that talking even with those they love and know well is emotionally painful. This especially may be the case if they are aware that they understand less and remember much less than before. I recall a patient who began to dread

seeing even her adult children and grandchildren over the holidays; she feared that she bored them. Psychiatrists may help these patients with AD by acknowledging the truth of such concerns. By validating their concerns, as opposed to dismissing them, psychiatrists may paradoxically enhance their self esteem. This implies, of course, that the psychiatrist communicates genuinely and openly with his or her patients. This may also improve patient alliance with the psychiatrist, and as a result, a patient with AD may feel he or she can divulge greater fears to the doctor. By openly discussing fears with the psychiatrist, who then listens and validates these feelings, patients with AD may feel safer with their psychiatrists and feel increased self esteem. These positive responses may both alleviate the social discomfort patients with AD feel and enhance their confidence in

themselves when they are with others.

Cognitive stimulation.

Cognitive stimulation may be beneficial to patients with AD by increasing activity in areas of the brain that are healthy, thus possibly creating "brain reserves" the patient can rely on as other parts of the brain deteriorate.¹¹ Yet, as with an exercise prescription, prescribing cognitive stimulation may possibly cause harm. One expert says that the present findings that older adults can have cognitive benefits from short-term mental training for at least five years "do not prove that crossword puzzles and Sudoku games will prevent AD, in spite of how these data are interpreted by the public."¹² Accordingly, while these exercises may or may not help the patient with AD, caregivers may feel guilty if they do not push these patients to engage in cognitive stimulation regularly. Even if a caregiver does not feel guilty, cognitive stimulation exercises may cause the patient to feel anxious and stressed, especially as the patient's cognitive functioning declines and the exercises become more difficult. If this is the case, both the caregiver and the patient may be better off spending quality time together doing some other type of activity they *both* enjoy.

PHARMACOLOGICAL INTERVENTIONS

Psychotropic medications. In most instances, aside from chiefly the anti-AD medications, other psychotropic medications have not been as substantially tested in the AD population.¹³ Psychiatrists generally should try a second or third anticholinesterase medication if the patient cannot tolerate the first or second, because the mechanisms of actions of these drugs and their benefits and side effects differ from one another.¹⁴ Many psychiatrists also

use memantine during the earliest stage of AD if the patient cannot tolerate any of the anticholinesterases.¹

The uncertainty (and difficulty) of deciding what, if anything, to do for a patient with AD increases as the symptoms of illness increase. A paradigmatic example is patients with AD who are depressed. That a psychiatrist can make the diagnosis of depression in a patient with AD is significantly in doubt.¹⁵ Signs and symptoms of AD and depression overlap. However, if a psychiatrist construes symptoms as indications of depression, this may increase the extent to which he or she treats the patient, thus benefitting patients with AD when they have depression.^{16,17} How far should a psychiatrist go to try to relieve a depressed patient with AD if the depression itself is open to doubt? Four drugs have been shown in randomized, controlled trials to be effective for depression in patients with AD: citalopram, sertraline, clomipramine, and the monoamine oxidase inhibitor (MAOI) moclobemide.¹⁷ Psychiatrists should clearly start with one of the serotonin reuptake inhibitors due to their decreased side effects, but if a depressed patient with AD does not respond or only partially responds, then the psychiatrist should consider switching to another drug or augmenting therapy. Even electroconvulsive treatment (ECT) may be effective in this patient population, though, due to its effects on memory, it usually should not be used.¹⁷

A paradigmatic model for psychiatrists in this situation may be similar to a model used when deciding whether or not to use atypical antipsychotics. Even with their black box warnings due to increased risk of serious morbidity and death in the elderly,

psychiatrists may use atypical antipsychotics when necessary to maintain or enhance the quality of their AD patients' lives. Psychiatrists should consider any medication's relative benefits and risks, especially in the contexts of the magnitude and rate of progression of the AD and the wants of the patients and their caregivers.

A final factor that should be preeminent when deciding whether or not to prescribe an off-label medication to a patient with AD may be difficult for some psychiatrists to accept: their level of personal comfort. It is my opinion that this factor should be an "absolute." I fear that if I prescribe a medication that lies outside my expertise, I may feel irrationally angry at a patient, consciously or unconsciously, for "causing me" to have this fear,^{18,19} and, without intending to, I may take this out on him or her in some way. If I think a drug may be beneficial and the patient wants this drug, I may refer this patient to a psychiatrist who has expertise using this particular drug and help the patient contact this psychiatrist, if necessary.

Patient participation in a clinical trial. In a recent conference presenting cutting-edge research on AD, Pierre N. Tariot, a leading AD expert, stated that he thought that doctors have a moral obligation to raise with patients with AD the issue of entering a research protocol.²⁰ Patients with AD may or may not benefit from being in a study; for research to be conducted, there must be clinical equipoise.²¹ This means that physicians cannot know which arm of a study, if either, will benefit participants more. Patients may, however, want to enter a trial, not because it will help them but because it ultimately will help others. Thus, psychiatrists should discuss all aspects of

participating in a clinical trial, positive and negative, to give patients an opportunity to make an informed decision.

In addition to keeping these patients optimally informed, psychiatrists should be aware that patients with AD may believe that it is likely they will benefit from participating in a clinical trial. This mistaken belief is known as the *therapeutic misconception*.²² This misconception may be particularly likely in patients whose abstract thinking is impaired, but it can occur in their caregivers just as well, who may magnify the potential gains due to hope.

Often, patients with AD may participate in research even after they have lost the capacity to consent.^{23–25} Under these circumstances, usually persons legally empowered to make decisions for the patients in clinical contexts can decide whether they can enter a research protocol.²⁶ The requirements to be able to participate and the procedures that must be applied in different studies for patients with AD tend to be analogous to those that must be applied to children. The requirements and procedures increase proportionately according to the participants' potential risks.²⁶ This similarity makes sense in that both children and patients with AD are cognitively impaired. Yet, psychiatrists should keep in mind that unlike children, patients with AD have lived long lives and have established firm values, often critically important to them. Due to this difference between children and patients with AD, it may be that patients with AD should be permitted to participate in research even if they would not be permitted to participate if they were children.

Legally, the conditions under which people with AD can

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participate in research differ from state to state, and these differences are sometimes substantial.²⁶ These differences may raise this question: To what degree, if any, should psychiatrists help patients with AD search state laws or “state shop” so that they can find a study in which they can participate? Psychiatrists can, in any case, help these patients find research opportunities that are available.²⁷ Psychiatrists also, ideally, should discuss this possibility with patients and their caregivers as early in these patients’ illnesses as they can. It may be helpful additionally for these patients to issue advance research directives.²⁸ This instrument documents a patient’s desire to participate in research if he or she later loses the capacity to express this.²⁹

The most controversial question psychiatrists can encounter, perhaps, is whether to help a patient with AD enter a study when the patient has not said previously that this is what he or she wants, he or she no longer has the capacity to express this, and his or her caregiver believes the patient would want this. One author, referring to this situation, said, “For a family member who knows that his loved

one would want to participate in research because she is a fighter who would risk anything in the hope of a cure or because she was the type of person who would wish to help in the fight against this terrible disease, allowing that individual to participate in research reaffirms that the person he loves is still there, still living according to her values.”³⁰

CONCLUSION

Psychiatrists treating patients with AD face much uncertainty in regard to what interventions, if any, they should prescribe or even discuss when those interventions are not evidence-based. Even seemingly benign nonpharmacological interventions, such as exercise, increased social interactions, and cognitive stimulation, may have negative effects. Any intervention(s) a psychiatrist chooses to recommend to a patient with AD should be discussed openly, covering both negative and positive aspects, with the patient and his or her caregiver.

Some medications have been shown to be helpful in AD only anecdotally. By discussing even these medications with their patients, psychiatrists demonstrate respect for their patients, which can improve therapeutic alliance and patient trust. Psychiatrists should also consider discussing participation by patients in a research protocol.^{31,32} The health of a patient with AD may or may not benefit directly from participating in research, but the patient may experience a significant sense of self worth from the knowledge that his or her participation may contribute to a greater good: discovering a cure for this devastating disease.

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